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EXAMINER	
BASI,N	
ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/518381	Yi Li et al
Examiner	**Group Art Unit**
Nirmal S. Bas:	1646

---The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address---

Peri d for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 6/29/01.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 23-96 is/are pending in the application.

Of the above claim(s) 30,32,40,42,50,62,64,74,76,82 & 84-96 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☐ Claim(s) 23-29,31,33-39,41,43-49,51,53-61,63,65-73,75,77-81 & 83 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

DETAILED ACTION

1. Preliminary amendment filed 3/3/00 (paper number 3), Reply to Restriction requirement filed 7/26/01 (paper number 7) has been entered.

2. Applicant's election with traverse of Group II (Claims 23-29, 31, 33-39, 41, 43-49, 51, 53-61, 63, 65-73, 75, 77-81 and 83) and, in Paper No. 7, is acknowledged. The traversal is on the ground(s) that it would not be a serious burden to examine the groups together. This is not found persuasive because a search of groups I-V would not be co-extensive particularly with regard to the literature search. An examination of the materially different, patentably distinct inventions in a single application would constitute a serious undue burden on the examiner. Claims 30, 32, 40, 42, 50, 62, 64, 74, 76, and 82 and 84-96 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The requirement is still deemed proper and is therefore made FINAL.

The applicant has indicated the request for rejoinder of method claims 30, 40, 50, 62, 74 and 82, should be examined together with the elected claims 29, 39, 49, 61, 73 and 81, if allowed, in light of *In re Ochiai, in re Brouwer* and 35 U.S.C. 103(b). This request must be submitted upon the indication of the allowability of the product claims.

3. **Objections**

The disclosure is objected to because of the following informalities:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78)

as well as the relationship of instant application to the parent. Parent Application 08/852,824, is now U.S. Patent Number 6,060,272, issued May 9, 2000, and must be indicated as such.

Applicants are required to use the heading "Brief Description of the Drawings" to describe the drawings. See MPEP 608.01(f). On page 4, Applicant has written "Brief Explanation of the Accompanying Drawings".

Appropriate correction is required.

4. The disclosure is objected to because of the following informalities:

Applicant has disclosed that clone 209004 was deposited but has not indicated the address of where it was deposited (see page 7). The specification should be amended to reflect the correct address for the ATCC and deposit information.

Further, the claims require availability of the clone 209003 indicated as deposited with ATCC. Applicant must provide evidence that clones listed in instant application will be available under the criteria (I)-(V) listed below. Although, the aforementioned cDNA if available today from ATCC, may not be available in the future. An enabled ATCC deposit would satisfy the requirements of 35 USC §112, first paragraph.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or Declaration by Applicants or someone associated with the patent owner who is in a position to make

such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(I) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(II) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

(III) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(IV) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(V) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803-1.809 for additional explanation of these requirements.

5. ***Claim Rejection, 35 U.S.C. 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 57, 69, 77, 78-81 and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 77 is indefinite because it is not clear which amino acids comprise the transmembrane domain of SEQ ID NO:4 so as to allow the metes and bounds of the claims to be determined. The specification describes transmembrane regions as being designated as TM1-TM7 but discloses no further details of said regions as they specifically pertain to instant polypeptide.

Claims 57, 69 are indefinite because it unclear what "activity" the G-protein coupled receptor has so as to allow the metes and bounds of claim to be determined. The "activity" of the G-protein coupled receptor has not been disclosed in the claims nor the specification.

Claims 78-81 and 83 are indefinite for depending on an indefinite claim.

Claim Rejections - 35 USC § 101 and 35 USC § 112, 1st paragraph

The following is a quotation of 35 U.S.C. 101:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 23-29, 31, 33-39, 41, 43-49, 51, 53-61, 63, 65-73, 75, 77-81 and 83 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to a isolated polynucleotide comprising:

A) 30, 50 or 150 contiguous nucleotides of SEQ ID NO:3, sequence 90% or 95% identical to 30, 50 or 150 contiguous nucleotides of SEQ ID NO:3,

B) polynucleotide at least 90% or 95% identical to a nucleic acid encoding 50 contiguous amino acids of SEQ ID NO:4 (ii) polynucleotide comprising a nucleic acid encoding 30 contiguous

amino acids of SEQ ID NO:4 which binds antibody having specificity to the polypeptide of SEQ ID NO:4, polypeptide of B having G-protein coupled receptor activity

C) polynucleotide encoding transmembrane region of SEQ ID NO:4

Further, dependent claim are drawn to expression vectors comprising claimed DNA, cell transformed with said DNA and process for producing protein using said cell.

A "specific utility" is a utility that is specific to the subject matter claimed, as opposed to a "general utility" that would be applicable to the broad class of the invention. A "substantial utility" is a utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. A "well established utility" is a utility that is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. A "well established utility" must also be specific and substantial as well as credible.

Based on the record, there is not a "well established utility" for the claimed invention. Applicant has asserted utilities for the specifically claimed invention of claims 23-29, 31, 33-39, 41, 43-49, 51, 53-61, 63, 65-73, 75, 77-81 and 83. The utilities disclosed in the specification are based on methods using receptor polypeptides and polynucleotides as a target for diagnosis and treatment in receptor-mediated and related disorders and for drug-screening methods using receptor polypeptides and polynucleotides to identify agonists and antagonists for diagnosis and treatment. The specification discloses:

a) EBI-2 (G protein coupled receptor of SEQ ID NO:2) has about 25% identity and 49% similarity to the EBI-1 gene over an approximately 350 amino acid stretch, page 6. EDG-1 (G protein coupled receptor of SEQ ID NO:4, herein referred to as EDG-1) has about 24% identity and 73% similarity to the EDG-1 orphan G-protein coupled receptor (seq id NO:18), page 6. Both EBI-1 and EDG-1 are found in a variety of tissue.

In light of the specification the skilled artisan can speculate that EDG-1 receptor is a seven transmembrane protein belonging to the G-protein coupled receptor super family. However, no disclosure is provided within the instant specification on what specific function a putative EDG-1 receptor protein possesses, or how to specifically assay for such, ligands that bind, promoters that activate, nor are any disease states disclosed that are directly related to EDG-1 receptor dysfunction. There is no disclosure in the specification of ligands that bind to EBI-1 receptor. Mudroch et al (Ref. A, see previous office action) discloses, the superfamily of G-protein-coupled receptors are highly divergent in their effects and include receptors for hormones, neurotransmitters, paracrine substances, inflammatory mediators, certain proteinases, taste and odorant molecules, and even photons and calcium ions (page 3032, introduction). Members of a sub-family of G-protein-coupled receptors are also highly divergent in their effects, as highlighted by Mudroch et al, in the discussion of cytokine G-protein-coupled receptors (see pages 3032-3039). The utility of EDG-1 G-protein coupled receptor cannot be implicated solely from homology to known G-protein coupled receptors because the art does not provide teaching stating that all members of a sub-family of G-protein coupled receptors must have the same effects, the same ligands and be involved in the same disease

states, the art discloses evidence to the contrary. For example, Mudroch et al discloses even though CCR6 is a member of the chemokine G-protein coupled receptors family and IL-2 was shown to up-regulate CCR6 mRNA recent data contradict this finding, and as a consequence, the effect of IL-2 on CCR6 expression remains uncertain (page 3035, second column, first paragraph). Further, the unpredictability of determining the G-protein associated with specific G-protein coupled receptors is highlighted by Watson et al (Ref B, page 5, third paragraph, see previous office action), who disclose,"Site directed mutagenesis, deletions and chimeric receptor studies have been used in an attempt to identify the region of the β2 adreoceptor that couples with Gs. This work has highlighted a sequence of ~8 amino acids in the N-terminal and ~12 amino acids in the C-terminus of the third transmembrane loop as important determinants of this interaction. However, it appears that additional regions of the receptor also participate in the binding to the G-protein, most notably in the second intracellular loop, and that it is the overall 3-dimensional structure of the receptor on the cytoplasmic side of the membrane that is important for the interaction with G-protein. It has therefore not been possible to identify consensus amino acid sequences that confer G-protein specificity, and thus G-protein interactions cannot be predicted from the primary amino acid sequence", (Ref B, page 5, third paragraph). Therefore the disclosure of Watson predicts, using the primary structure of the G-protein coupled receptor the skilled artisan cannot predict its associated G-protein. The EDG-1 receptor of instant invention is considered by the examiner to be a member of the orphan receptor of G-protein coupled receptors i.e. seven transmembrane receptor with no known endogenous ligands. Watson et al devote a whole chapter to orphan G-protein coupled

receptors and group them separately because even though the orphan receptors posses a certain degree of homology to G-protein coupled with known function, the orphan receptors require further research before they can be classified into one of the groupings of known G-protein coupled receptors (Ref B, pages 223-230). Further, a position that the EDG-1 receptor is related to G protein coupled receptors, and therefore must have the same biological activity and be classified as EDG type receptor, can not be made, without the knowledge of the endogenous ligand for EDG-1 receptor. The specification compares the EDG-1 receptor of SEQ ID NO:18, which itself is an orphan receptor without a function. The receptor of SEQ ID NO:18 can not be used to infer a function on EDG-1 receptor. The assumption that an orphan receptor be placed in a particular group is not always true as highlighted by the statement Watson, who states, "It was originally claimed that the human homologue of RDC1 codes for VIP receptor, but this is no longer thought to be correct" (Ref B, page 228). Therefore, since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed EDG-1 receptor and fragments thereof, further experimentation is necessary to attribute a utility to the claimed polypeptides and fragments thereof.

The instant application does not disclose the biological role of EDG-1 receptor or its significance. The utilities are not considered to be specific and substantial because the specification fails to disclose any particular function or biological significance for the EDG-1 receptor of the instant invention. The disclosed protein, whose cDNA has been isolated, is said to have a potential function based upon its amino acid sequence similarity to other known proteins.

After further research, a specific and substantial credible utility might be found for the claimed isolated compositions. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

Claims of instant invention are drawn to nucleic acid encoding a polypeptide with, as yet, undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the claimed receptor of the instant application was, as of the filing date, useful for diagnosis, prevention, and treatment of disease, such as cancers etc.

Until some actual and specific significance can be attributed to the protein identified in the specification as EBI-2 receptor, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The DNA of the instant invention and the protein encoded thereby are compounds which share some structural similarity to receptor proteins having GPCR domains based on sequence similarity. As disclosed by the specification, the family of proteins related to EDG-1 receptor may have diverse effects and bind a diverse number of ligands. The family of proteins having GPCR like domains have different levels of expression, and play roles in the pathogenesis of various diseases. Although the family of receptor proteins having EDG-1 receptor like domains may share some common structural motifs, various members of the family may have different sites of action and different biological effects. In the absence of knowledge of the ligand for EBI-2 receptor or the biological significance of this protein, there is no immediately evident patentable use. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research. Such a use has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for EDG-1 receptor, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

In conclusion, the utilities asserted by Applicant are not specific or substantial. Since no specific function of the polypeptide of instant invention is known, and the hypothesized function

is based entirely on conjecture from homologous polypeptides, the asserted utilities are not specific to instant polypeptide, but rather are based on family attributes. Neither the specification nor the art of record disclose the protein of SEQ ID NO:4 or fragments thereof useful to identify drugs that affect said protein and modulate its activity. Similarly, neither the specification nor the art of record disclose any instances where disorders can be effected by interfering with the activity using the EDG-1 receptor or fragments thereof. Thus the corresponding asserted utilities are essentially methods of using EBI-2 receptor to identify disease states associated with EDG-1 receptor disfunction and as targets for drug discovery. Therefore the asserted utilities are essentially methods of testing for or for potentially treating unspecified, undisclosed diseases or conditions, which does not define a "real world" context of use. Treating or testing for compounds that interact with EDG-1 receptor which may be implicated in an unspecified, undisclosed disease or condition would require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the claimed EDG-1 receptor and fragments thereof, further experimentation is necessary to attribute a utility to the claimed polypeptides and fragments thereof. See Brenner v. Manson, 383 U.S. 519, 535-36, 148 USPQ 689, 696 (1966) (noting that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing", and stated, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful

conclusion."). Further since the nucleic acid encoding EDG-1 receptor or the encoded polypeptide are not supported by either a specific and substantial asserted utility or a well established utility, it follows that vectors or cells comprising claimed polynucleotide and the methods of using said vectors or cells also not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above

9. Claims 23-29, 31, 33-39, 41, 43-49, 51, 53-61, 63, 65-73, 75, 77-81 and 83 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Since neither the specification nor the art of record disclose any activities or properties that would constitute a "real world" context of use for the EDG-1 receptor and fragments thereof, further experimentation is necessary to attribute a utility to the claimed method of using the EBI-2 receptor polypeptides and fragments thereof.

Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Further, many of the polypeptides, encoded by the nucleic acids of instant invention, may be inactive or unrelated to the EDG-1 receptor of instant invention, being devoid of its characteristic

structural and functional features. The specification does not disclose a utility for or how to use said inactive or unrelated polypeptides. Due to the large quantity of experimentation necessary to identify the polypeptides with the structural and functional features of instant invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said polypeptides, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of SEQ ID NO:4 are also encompassed by the claim), and the breadth of the claim which fail to recite structural and functional limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Furthermore, the specification does not reasonably provide enablement for the scope of use of polypeptides comprising fragments of claimed receptor, which encompass variants of the polypeptide of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The specification discloses a polynucleotide, SEQ ID NO:3, which encodes the polypeptide of SEQ ID NO:4. The specification does not teach how to make functional EDG-1 receptor variants or to use inactive variants. The specification does not teach how to make active variants comprising transmembrane regions and how to use inactive variant proteins and inactive proteins comprising transmembrane regions. The prior art teaches that amino acid substitutions produce unpredictable results in a structurally related protein. Furthermore, neither the specification nor the prior art provide any guidance as to which amino acids could be altered, nor does the

specification provide any guidance as to how the skilled artisan could use an inactive EDG-1 receptor variants. Also there is no disclosure of the critical special technical feature encompassed by an active EDG-1 receptor or variants, or how the critical special technical feature encompassed by polypeptide comprising fragments of SEQ ID NO:4 or variants of EDG-1 receptor GPCR relates to function. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation that an EDG-1 receptor variant could be used for any purpose. It is noted that numerous fragments comprising portions of the EDG-1 receptor would not have the activity specific for the EDG-1 receptor of SEQ ID NO:4 nor would they have any of the functional or structural characteristics of said receptor. Applicant has not disclosed how to use said "fragment" containing receptors.

Claims 23-29, 31, 33-39, 41, 43-51, 53, 55-64, 66, 68-77, 79, 81-89, 91, 93-97 and 99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification and claims fail to disclose the activity of the claimed genus of polypeptides, the critical special technical feature of the polypeptides or how the critical special technical feature encompassed by the fragments and variants of EDG-1 receptor relates to function. The claims encompass polynucleotides encoding proteins which are structurally and functionally unrelated to the protein of SEQ ID NO:4. Therefore instant specification fails to provide sufficient descriptive

information, such as definitive structural/ functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed.

The claims are drawn to a isolated polynucleotide comprising:

A) 30, 50 or 150 contiguous nucleotides of SEQ ID NO:3, sequence 90% or 95% identical to 30, 50 or 150 contiguous nucleotides of SEQ ID NO:3,

B) polynucleotide at least 90% or 95% identical to a nucleic acid encoding 50 contiguous amino acids of SEQ ID NO:4 (ii) polynucleotide comprising a nucleic acid encoding 30 contiguous amino acids of SEQ ID NO:4 which binds antibody having specificity to the polypeptide of SEQ ID NO:42, polypeptide of B having G-protein coupled receptor activity

C) polynucleotide encoding transmembrane region of SEQ ID NO:4

Further, dependent claim are drawn to expression vectors comprising claimed DNA, cell transformed with said DNA and process for producing protein using said cell.

The claims, as written, polynucleotides encoding polypeptides which vary substantially in length and also in amino acid composition. The instant disclosure of a polynucleotide of SEQ ID NOs:3 encoding the polypeptide of SEQ ID NO:4 (EDG-1) does not adequately describe the scope of the use of the claimed genus of polynucleotides encoding polypeptides, which encompasses a substantial variety of subgenera including full-length proteins, mature proteins, epitope region bearing polypeptides, chimeric proteins, fusion proteins, and variants (with no known or disclosed function). Further, polynucleotides encoding polypeptides, comprising fragments of SEQ ID NO:4, may also,

be completely unrelated to the polypeptide of SEQ ID NO:4. A description of a genus of polypeptides may be achieved by means of a recitation of a representative number of polypeptides, defined by amino acid sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural and functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. For example, what regions and fragments of the polypeptide of SEQ ID NO:4 contain a definitive structural feature required for protein function? The specification proposes to discover other members of the genus by using screening assays and techniques involving probes, primers, hybridization. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed. No identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific

polypeptide and nucleotide sequences and the inability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe, enable and use the genus as broadly claimed. The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and, therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. However, in the current instance, **there is no clear evidence of activity possessed by the claimed genus of polypeptides, the critical special technical feature of the polypeptides or how the critical special technical feature encompassed by the genus claimed relates to function.** Because of the lack of guidance in the prior art and current application, one skilled in the art could not predict if the variants or polypeptides containing fragments of SEQ ID NO:4 have the same activity as EDG-1 GPCR, since no activity is disclosed, or if they contain the domain(s) of SEQ ID NO:4, containing the critical special technical feature of the EDG-1 GPCR, since no critical special technical feature is disclosed. The breadth of the claim come from encompassing a protein, the active form of which is not known, apart from the polynucleotide of SEQ ID NO:3, encoding the polypeptide of SEQ ID NO:4.

Pertaining to the polynucleotide encoding polypeptide comprising transmembrane regions, the specification does not disclose the specific transmembrane regions protein recited in the claim. he skilled artisan cannot envision the detailed chemical structure of the encompassed proteins and,

therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. It is acknowledged that the skill of the artisan in the molecular biology art is high. It is further acknowledged that domains may be identified as potential transmembrane, but there is no clear disclosure the speciifc amino acid residues corresponding to the transmembrane regions. Because of the lack of guidance in the prior art and current application, one skilled in the art could not predict if the speciifc residues of the transmembrane domain, since the speciifcation discloses the sequencing accuracy of SEQ ID NO:3 may only be slightly more than 97%. The breadth of the claim come from encompassing a protein, the form of which is not known.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid or polypeptide is itself is required.

See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore only the use of isolated polynucleotide, SEQ ID NO:3, encoding the polypeptide shown in SEQ ID NO:4, meets the written description provision of 35 USC 112, first paragraph.

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
October 9, 2001

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